Chapter 2

Healthcare: the economic context

Introduction

2.1 The great disparities between levels of health across the world correlate in general quite closely with the degree of socio-economic development of different countries. Not surprisingly, people living in poorer countries tend to have significantly higher rates of morbidity[1] and mortality than those living in wealthier countries. Historically, in the developed world, improved levels of health have been closely correlated with social and economic development.[2] In the more recent past, the same has held true in countries that are still classed as developing, and this relationship is likely to continue to hold in the future. However, certain countries or regions, such as Sri Lanka, Cuba and some states in India, have achieved improvements in health disproportionate to the development of their economy. This is usually because of the healthcare and educational systems adopted as a result of specific government policies.

2.2 Research into the diseases affecting developing countries has to be seen within the context of their socio-economic conditions. Many would regard the wide disparities in wealth between countries, and often between different groups within countries, as inherently unethical and consider that redressing these imbalances should be given a high priority. It is highly likely that a more equitable distribution of resources (wealth) would lead to much greater equality in the health status of different populations. However, some medical or health-related interventions that will improve health status, including vaccines against important infectious diseases such as AIDS, TB and malaria, could be deployed in advance of economic development, and may even promote such development.

2.3 However, it would be inappropriate to introduce or promote new interventions in developing countries without prior research into the risks and benefits for the populations in those countries. Even interventions that have been shown to be effective in specific populations will need to be carefully evaluated before being introduced into other areas where the local environmental, ecological and genetic profiles are very different. This kind of research in healthcare is an important priority for developing countries to assist in the proper selection and use of disease-reducing interventions and often needs to be conducted in the country where use of the intervention is proposed. Such research is often expensive and one form of assistance that several developed countries give to developing countries is the funding and provision of scientific and technical support to help promote and foster the conduct of appropriate research.

2.4 In this chapter we first review the disparities in the levels of health between countries and then describe the variation in the resources they have available for healthcare and promotion. Against this background we then discuss the measures involved in developing interventions for preventing or treating disease.

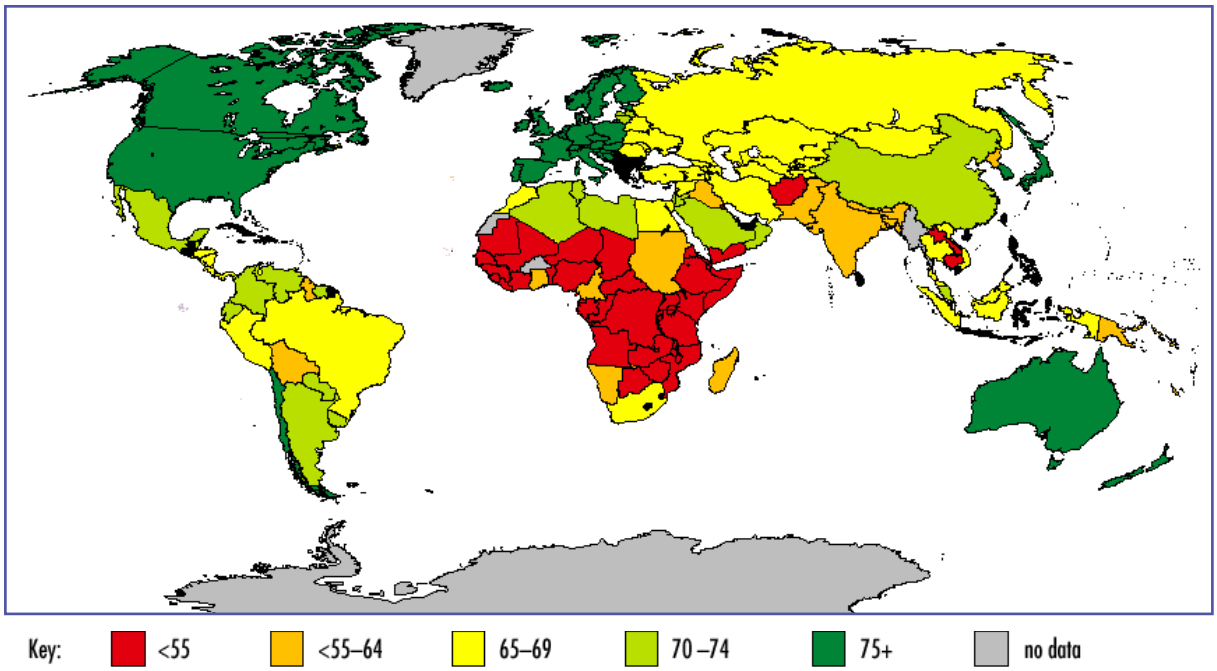
Variations in life expectancy between countries

2.5 The wide disparity in levels of morbidity and mortality between countries can be illustrated by examining the variation in life expectancy at birth. Figure 2.1 is a world map showing the average number of years that a live-born baby might expect to live in different countries.[3] Most of those born in the developed world can expect to live in excess of 70 years, whereas in the majority of African countries average life expectancy is less than 55 years, while in others it is less than 40 years (for example Zambia 38.5; Malawi 37.8 and Sierra Leone 34.3).[4]

1 Levels of sickness and ill health.
2 See for example, McKeown T (1976) **The Role of Medicine: Dream, Mirage or Nemesis**, Nuffield Provincial Hospitals Trust, London.
3 Based on estimated age-specific mortality rates in 1997.
4 World Health Organization (2000) **The World Health Report 2000. Health Systems: Improving Performance**, WHO, Geneva.

Figure 2.1:

Global map of expectation of life at birth



Redrawn from the World Bank Group's web site at: http://knowledge.worldbank.org/scripts/esrimpa.dll?name=gisonline&cmd=start map&view=21. (areas that were unclear on the original are shown in black)

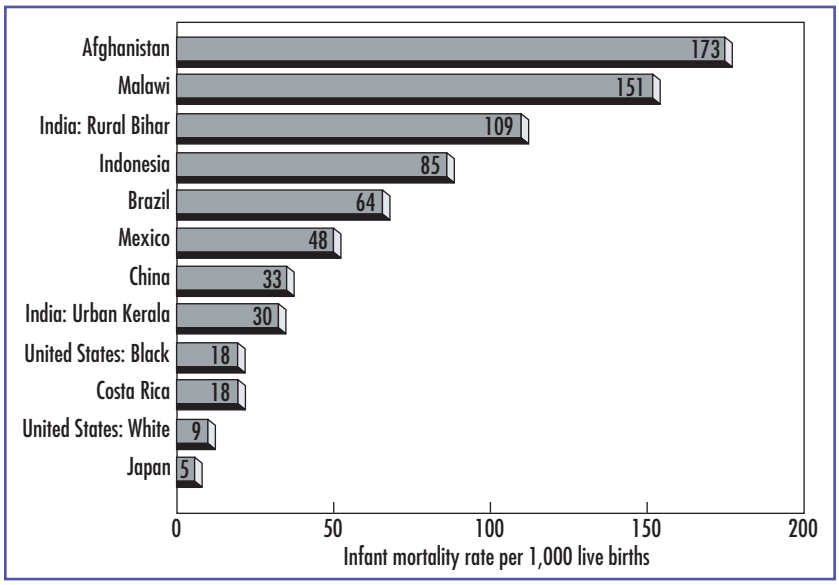
2.6 In an attempt to include morbidity as well as mortality in a summary measure of health, the World Health Organization (WHO) has calculated the average 'disability-adjusted life expectancy' for 191 countries.[5] This is most easily understood as the expectation of the total life lived in full health. Thus, it takes account of years lived with sickness and disease by discounting some of that time according to the seriousness of such conditions. The differences between countries based on disability-adjusted life expectancy are even greater than those based on simple expectation of life at birth. The estimates range from 74.5 years for Japan to 25.9 years for Sierra Leone. The majority of developed countries have estimates in excess of 70 years[6] while many African countries have estimates below 40 years.[7] Life expectancies in eastern and central Africa are particularly low because of the devastating effects of the current AIDS epidemic. In general, the levels of health in Asia and Latin America are intermediate between, on the one hand, Japan, North America and Western Europe and, on the other hand, Africa. However, the variation between different countries in each of these regions is substantial. [8]

2.7 An important reason for the differences in life expectancy is the variation in mortality rates among infants and young children. The scale of these differences is illustrated by infant mortality rates[9] in a selection of different countries (Figure 2.2). These range from 5/1000 for Japan to 173/1000 in Afghanistan.[10] There are also substantial variations within countries, as for example between the states of Bihar and Kerala in India and between African-Americans and

5 World Health Organization (2000) **The World Health Report 2000**. **Health Systems: Improving Performance**, WHO, Geneva.
6 For example France 73.1, UK 71.7, US 70 years
7 For example Kenya 39.4, Tanzania 36.0, Zimbabwe 32.9, Uganda 32.7, Zambia 30.3, Malawi 29.4 years.
8 For example, in Latin America disability-adjusted life expectancies range from 68.6 years in Chile, 68.4 in Cuba and 59.1 in Brazil to 53.3 in Bolivia. In Asia, it ranges from 69.3 years in Singapore and 62.8 in Sri Lanka through to 49.5 in Nepal and 37.7 in Afghanistan.
9 The number of children dying in the first year of life, per 1000 children born.
10 Commission on Health Research for Development (CHRD) (1990) **Health Research: Essential Link to Equity in Development**, Oxford University Press, New York.

Figure 2.2:

Infant mortality rate in selected populations



Reproduced with permission from Commission on Health Research for Development (CHRD) (1990) **Health Research: Essential Link to Equity in Development**, OUP, New York.

whites in the US. Similar variability between countries is evident with respect to child mortality rates, as illustrated in Figure 2.3.[11]

2.8 Much of the difference between mortality rates in developed and developing countries is due to communicable diseases such as AIDS, tuberculosis, malaria, respiratory infections and diarrhoeal diseases. Figure 2.4 shows the disability-adjusted life years (DALYs) lost in three different regions of the world due to communicable diseases, non-communicable diseases and injuries.[12] Nearly three-quarters of the lost DALYs are attributable to communicable diseases in sub-Saharan Africa, compared to only about 10% of lost DALYs in many developed countries.

2.9 Until recently, when the effects of the AIDS epidemic began to be reflected in rising rates of mortality, life expectancies had been rising in most countries. They have continued to do so except, generally, in those countries worst hit by the AIDS epidemic, or those in which there has been war. The improvements in life expectancy are likely to be due to improved standards of living and important advances in the development of interventions to prevent or treat disease. The expanded programme of immunisation has been perhaps the most important contributor to lowering infant and child mortality rates. This has raised vaccination rates against some preventable diseases, such as polio and measles, to high levels in many countries. However, for many diseases that cause significant numbers of deaths during childhood, such as malaria, diarrhoeal diseases and respiratory infections, effective vaccines have not yet been developed.

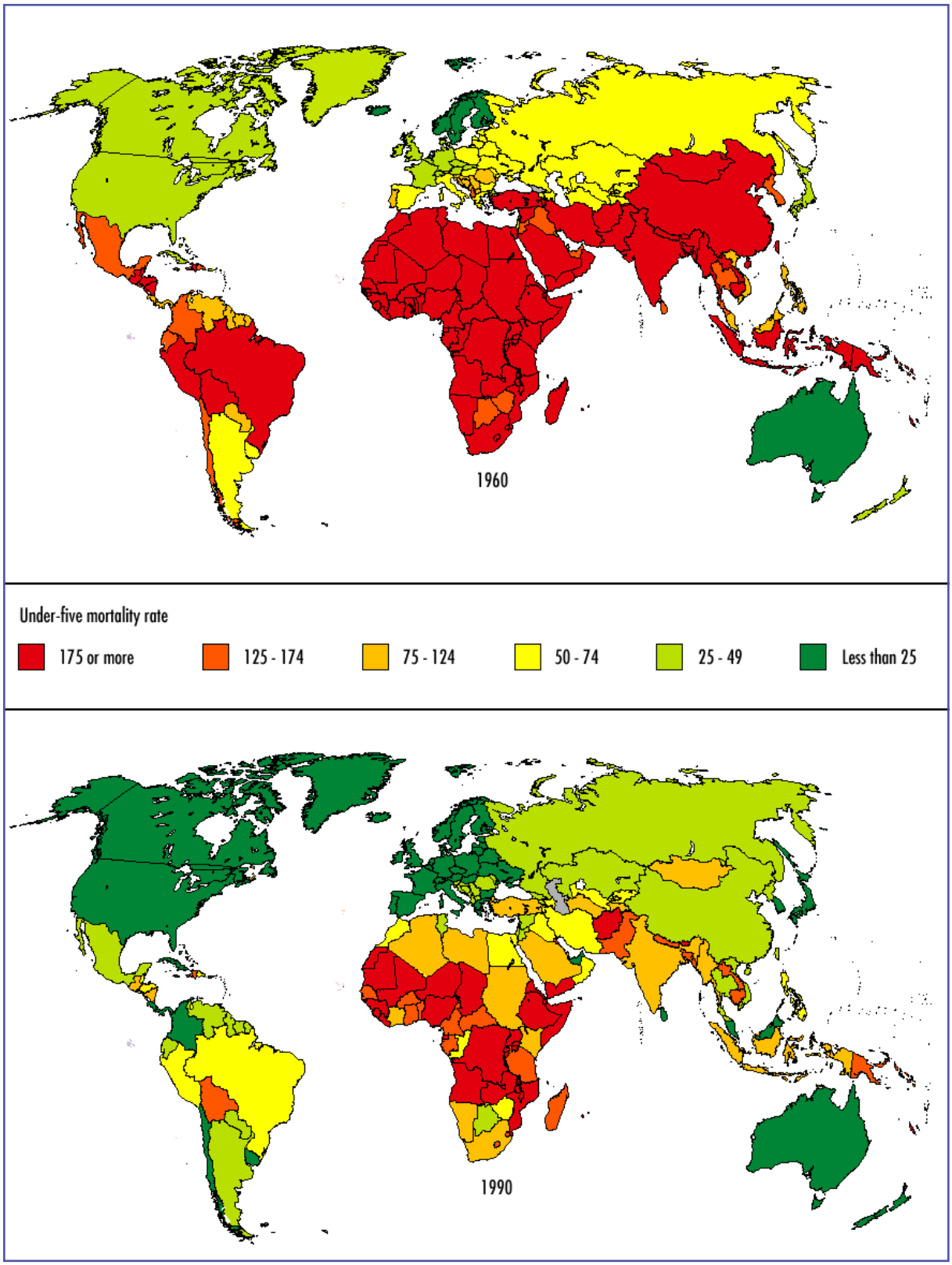
Variation in resources available for healthcare between countries

2.10 There is, in general, a strong association between life expectancy and economic development.[13] Figure 2.5 plots life expectancy at birth in relation to gross national product (GNP) per capita.[14]

11 The World Bank (1993) **World Development Report 1993. Investing in Health**, Oxford University Press, New York.
12 The World Bank (1993) **World Development Report 1993. Investing in Health**, Oxford University Press, New York.
13 Commission on Health Research for Development (CHRD) (1990) **Health Research: Essential Link to Equity in Development**, Oxford University Press, New York.
14 The GNP is the total value of all final goods and services produced for consumption in a country: it is a measure of a nation's total economic activity.

Figure 2.3:

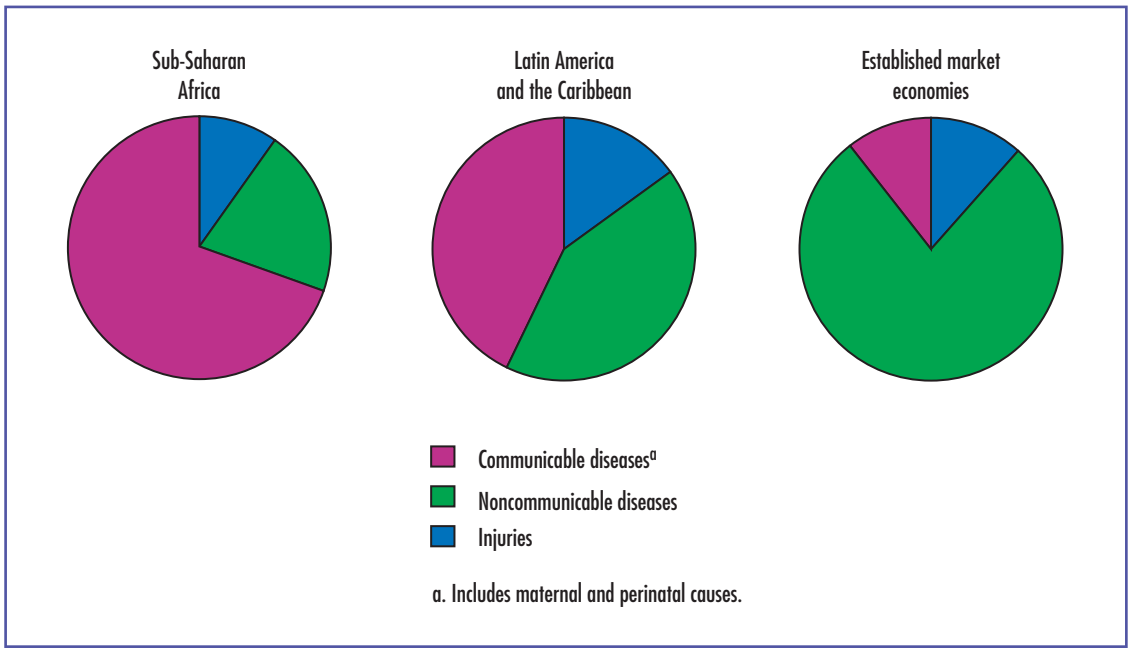
Child mortality by country, 1960 and 1990



Reproduced with permission from The World Bank (1993) **World Development Report 1993. Investing in Health,** Oxford University Press, New York.

Figure 2.4:

Distribution of disability-adjusted life years (DALYs) lost, by cause, for selected demographic regions, 1990 (percentage of total DALYs lost)



Reproduced with permission from The World Bank (1993) **World Development Report 1993. Investing in Health**, Oxford University Press, New York.

Figure 2.5:

Relationship between life expectancy at birth and gross national product per capita

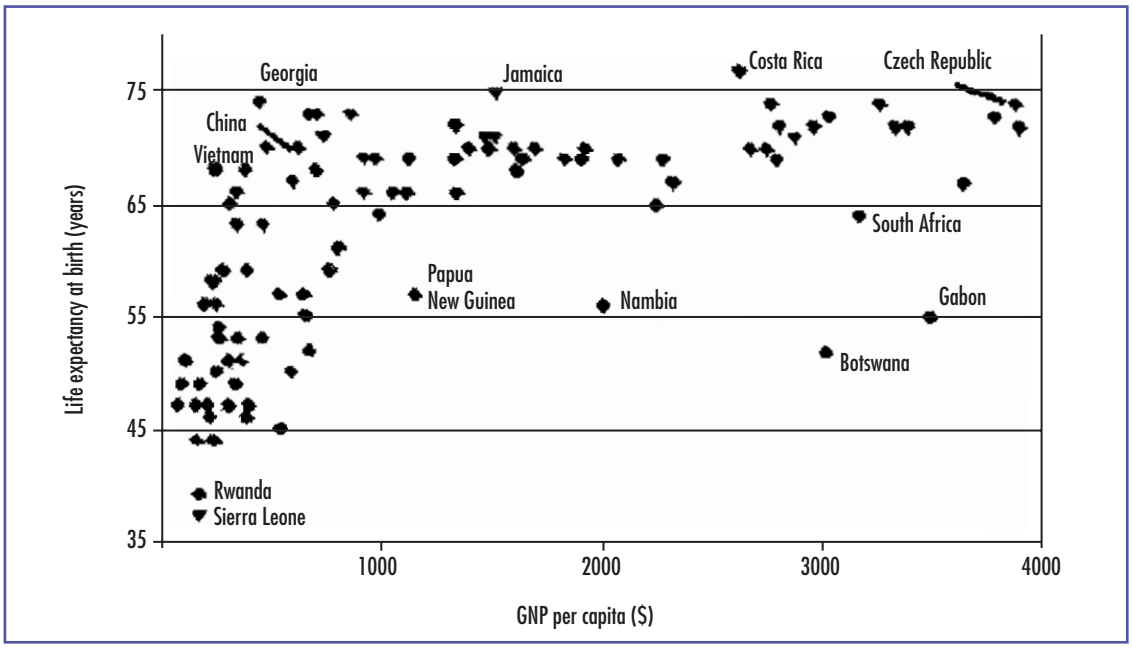


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Table 2.1

Expenditures on health and other health indicators in selected developed and developing countries

	Annual health expenditure per capita (internat. $[1])	Health expenditure as % GNP	Life expectancy at birth Males/females	Doctors /10^5 popn	Nurses /10^5 popn
United States	3724	13.7	73.8 /79.7	279.0	972.0
Japan	1759	7.1	77.6 /84.3	193.2	744.9
United Kingdom	1193	5.8	74.7 /79.7	164.0	497.0
Chile	581	6.1	73.4 /79.9	110.3	47.2
Brazil	428	6.5	63.7 /71.7	127.2	41.3
Cuba	109	6.3	73.5 /77.4	530.4	677.6
Afghanistan	89	3.2	45.3 /47.2	11.0	18.0
India	84	5.2	59.6 /61.2	48.0	45.0
Sri Lanka	77	3.0	65.8 /73.4	36.5	102.7
Uganda	44	4.1	41.9 /42.4	n/a	18.7
Sierra Leone	31	4.9	33.2 /35.4	7.3	33.0
Somalia	11	1.5	44.0 /44.7	4.0	20.0

Reproduced with permission from WHO (2000) **The World Health Report 2000. Health Systems: Improving performance.** WHO. Geneva and WHO Estimates of Health Personnel: Physicians, Midwives, Dentists and Pharmacists (around 1998) at http://makeashorterlink.com/?D2271283.

[1] International dollars' take into account the local purchasing power of the currency and in developing countries are thus generally higher than the expenditure in US$'s.

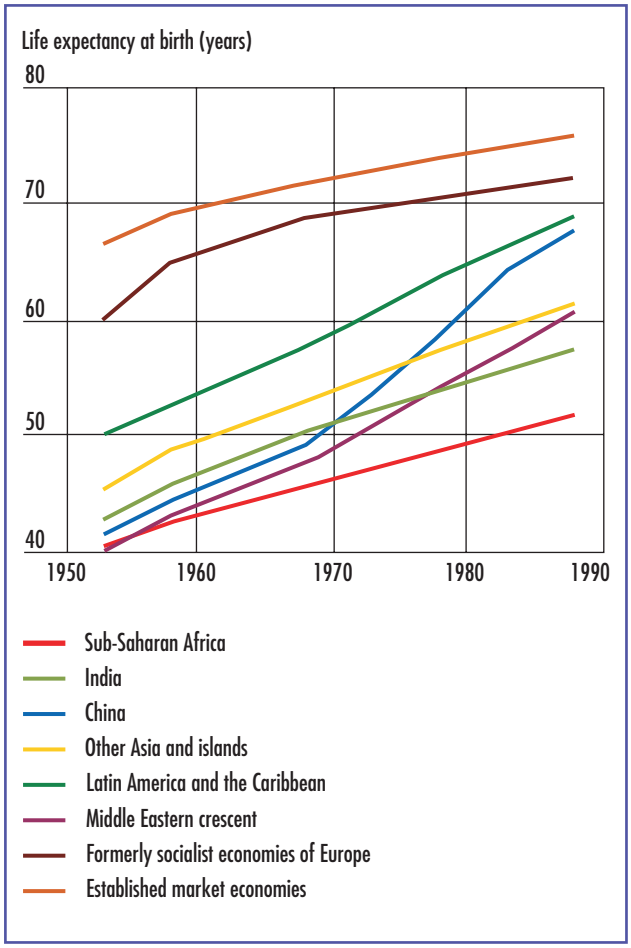
Though the relationship is not a simple one, the populations in countries with a low GNP per capita, and especially those with a GNP per capita of less than US$1000, tend to have much lower life expectancies than those in wealthier countries. Although there has been a substantial improvement in life expectancy over the last several decades in most countries,[15] there has been little change in the relative differences in life expectancy between regions of the world at different levels of economic development, as illustrated in Table 2.1 and Figure 2.6.[16]

2.11 The previous paragraphs have highlighted the wide differences in health between, and in some cases within, countries and pointed out the broad relationship between better health and more advanced socio-economic development. The level of expenditure that different countries devote to healthcare also varies widely. For example, it has been estimated that the US, which has approximately 5% of the world's population, is responsible for 50% of the annual global expenditure on healthcare.[17] In general, developing countries are able to devote a smaller proportion of their GNP to health than wealthier countries can. Furthermore, in absolute terms, the resources allocated are substantially less than in developed countries. This is reflected in the

15 Before the impact of the AIDS pandemic was reflected in life expectancy data (see paragraph 2.9).
16 The World Bank (1993) **World Development Report 1993**. **Investing in Health**, Oxford University Press, New York.
17 Bloom B (1999) The future of public health, **Nature**, 402: C63–4.

Figure 2.6:

Trends in Life Expectancy by Demographic Region, 1950–90



Reproduced with permission from The World Bank (1993) **World Development Report 1993. Investing in Health**, Oxford University Press, New York.

numbers of physicians and nurses per member of the population. For example, the number of physicians ranges from over 100 per 100,000 members of the population in more developed countries to less than 10 physicians per 100,000 members of the population in the least developed countries (Table 2.1).

2.12 Of course, the health of a population is determined not only by the resources devoted to healthcare and to preventive medicine, but also by investment in other important determinants of good health such as education, nutrition, water, sanitation and communication infrastructure. The lack of resources to develop these facilities, which are crucial if health benefits are to be sustained, further disadvantages developing countries. Even in those countries in which there are potentially more resources available to devote to infrastructure development, political leaders may sometimes have alternative priorities and allocate funds elsewhere.

The 10/90 disequilibrium: research expenditure and premature mortality

2.13 The disparity in expenditures on health research between developed and developing countries was highlighted in the 1990 report of the Commission on Health Research for Development.[18] This

18 CHRD (1990) **Health Research: Essential Link to Equity in Development**, Oxford University Press, New York.

group assessed the total funds that were being spent on research in different countries and examined the burden of ill health. Their analyses revealed a striking disparity between health needs and research expenditures. Using those countries with the lowest mortality rates as a benchmark, they proposed that differences from these rates in other countries represented potentially avoidable mortality. The amount of avoidable mortality[19] in developed and developing countries was calculated and compared to the estimated research expenditures on the respective health problems of each country. These calculations led to the estimates that 93% of the global burden of premature mortality is attributable to disease problems in developing countries but that about 95% of global expenditure on health research is directed at the disease problems of developed countries. Refinements of these estimates by the WHO Ad Hoc Committee on Health Research[20] supported the conclusion that the central problem in research on health is the '10/90 disequilibrium'. Namely, that of the US$ 50–60 billion spent world-wide each year on health research by both the private and public sectors, only 10% is devoted to the health problems of 90% of the world's population.[21] It is against such a background that research on health in developing countries must be considered.

2.14 The gross disparities in investment in research on health between countries are also reflected in the availability of those with appropriate training to conduct research on health. Despite the great need for research to determine the most effective interventions in developing countries, the indigenous capacity to conduct this research is severely limited. The lack of appropriate infrastructure, expertise and resources are major constraints. Externally-supported research that does not address this issue of development of capacity in research may greatly limit the long-term value of the research. In many respects such research is the equivalent of food aid, which does not provide the tools and skills to help the local population to become self-sufficient in growing their own food. Building capacity within developing countries will help those countries to set their own priorities for research and to conduct the most relevant research for local health needs.

2.15 As many developing countries have very limited resources, it is highly desirable that investments in healthcare focus on those interventions that are affordable, effective and accessible. This is best achieved by ensuring, so far as is possible, that health policy is evidence-based: only those interventions that are proven to be effective and affordable are introduced into the national health programme. To develop such an evidence base requires that the experience of other countries with particular interventions is taken into account. When the evidence is lacking, it will sometimes be necessary to conduct new or additional research in the relevant country. This will often be beyond a developing country's own resources and research which is externally sponsored may be the sole means of acquiring the necessary evidence.

The scope of externally-sponsored research

2.16 Whilst there is currently no central audit of research which is conducted in developing countries by external sponsors, organisations such as the US Food and Drug Administration (FDA) and Pharmaceutical Research and Manufacturers of America (PhRMA) monitor the amount of research and development (R&D) conducted abroad. The FDA has recorded a 16-fold increase in the number of foreign clinical investigators conducting research on new medicines in the decade 1990–2000. Numbers grew from 271 in 1990 to 4,458 in 1999.[22] The number of

19 In terms of years of life lost due to premature mortality.
20 World Health Organization (1996) **Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options**, WHO, Geneva.
21 Global Forum for Health Research (1999) **The 10/90 Report on Health Research 1999**, Global Forum for Health Research, Geneva.
22 DHHS Office of Inspector General (2001) **The Globalization of Clinical Trials. A Growing Challenge in Protecting Human Subjects**, Office of Evaluation and Inspections, Boston.

Table 2.2

Growth in domestic US R&D and R&D overseas

Year	Domestic US R&D ($ M)	US R&D Abroad ($ M)
2001	23,640.0	6,862.0
2000	19,986.7	5,692.2
1999	18,499.3	4,219.6
1998	17,222.5	3,839.0
1997	15,516.6	3,492.1

Source: PhrMA (2001) **Pharmaceutical Industry Profile 2001: Table 1: Growth in Domestic US R&D and R&D Abroad, Ethical Pharmaceuticals, Research-based pharmaceutical companies, 1970–2001.**

countries, monitored by the FDA, in which clinical investigators conducted research increased nearly three-fold from 28 to 79 for the same period, with the largest growth occurring in Latin America and Eastern European countries.[23]

2.17 In its Annual Survey for 2001, PhRMA gave a detailed account of R&D by research-based pharmaceutical companies. Although this showed recent dramatic growths in the investment and proportion of US R&D conducted abroad (Table 2.2), the proportion of overall R&D conducted in developing countries remains small, with the highest proportion of research carried out in the developing world taking place in Latin America (Table 2.3).

2.18 Audits of international research activity on specific diseases have also been conducted. For example, the Unit for Policy Research in Science and Medicine (PRISM) of the Wellcome Trust conducted an audit of malaria research.[24] Expenditure dedicated to research on malaria was found to be low compared with other areas of disease. For example, while the UK alone spent over $200 million on research on cancer in 1993, total expenditure for research on malaria *worldwide* was only $84 million. Analysis of research publications showed that active research was taking place in many areas of basic research into malaria, such as the mechanisms of action of medicines and disease transmission, but that there was less research in other areas, such as means of providing antimalarial treatment to populations in developing countries.

2.19 However, since the second half of the 1990s, this picture of international research activity has been reconfigured somewhat. This is due in part to the growing number of collaborations between the corporate and public sectors in the form of global public-private partnerships (GPPPs). These developed from recognition of market and 'public' failures in international public health and have allowed major investments in the area. Examples include the Medicines for Malaria Venture (MMV), one of the first public-private partnerships which found its origins in the failure of the market system to provide the required incentives for wide-scale R&D in new medicines for malaria.

23 DHHS Office of Inspector General (2001) **The Globalization of Clinical Trials. A Growing Challenge in Protecting Human Subjects**, Office of Evaluation and Inspections, Boston.

24 Anderson J, MacLean M and Davies C (1996) **Malaria Research. An Audit of International Activity**, Unit for Policy Research in Science and Medicine (PRISM), Wellcome Trust, London.

Table 2.3

US funded R&D conducted abroad by geographic area in 1999

Geographic area	Amount (US$ mil.)	Share (%)[1]
Canada	451.2	9.2
Latin America (inc. all Caribbean nations)	78.5	1.6
Western Europe (EC, European Free Trade Association and Switzerland)	3,569.2	72.9
Central and Eastern Europe (inc. ex-USSR)	21.6	0.44
Middle East (inc. Turkey)	3.5	0.07
Africa	4.1	0.08
Asia/Pacific (from Pakistan to SE Asia inc. China, Taiwan, and the Koreas)	19.7	0.40
Japan	711.1	14.5
Australia and New Zealand	45.4	0.93
Total	**4,904.2**	

[1]Percentages do not add up to 100 because of rounding.

Source: PhrMA (2001) **Pharmaceutical Industry Profile 2001: Table 9: R&D Abroad by Geographic Area, Ethical Pharmaceuticals, Company-financed, U.S.-Owned Research-based Pharmaceutical Companies, 1999.**

2.20 As in developed countries, a very wide range of research related to healthcare is conducted in developing countries, the majority of which is externally sponsored. The spectrum ranges from laboratory research into the causes of disease, through clinical research involving human participants which aims to determine the safety and efficacy of novel interventions, to feasibility and operational research, which is designed to determine if and how effective treatment can be delivered to the broader patient population (see Box 2.1). The various types of research conducted are discussed further in Appendix 2.

Setting priorities for research

2.21 The question of how a country sets its priorities for research in healthcare is particularly important in developing countries because national resources for research are generally very limited. The setting of national priorities for research is a complex process involving national and international research objectives, institutions and individuals. Clearly, the greater the capacity of a country to conduct its own research and to have systems in place to determine its own priorities, the easier it will be to ensure that the questions posed by externally-funded research are appropriate and relevant to national health needs. It will be more difficult for government and external sponsors to collaborate effectively if there is no clear picture of the priorities for research within a country.

2.22 The capacity of developing countries to set their own priorities for research varies widely. Some countries make use of WHO's recommendations by adopting those parts that are relevant to

BOX 2.1 Examples of the kinds of research conducted in developing countries

Basic research

A genetic transformation system for the mosquito *Anopheles stephensi*, a major carrier of malaria in urban areas of the Indian subcontinent has now been developed.[1] Such developments in understanding the interactions between malaria parasites and the mosquito vectors of malaria will allow further research into the molecular aspects of malaria parasite transmission and new control mechanisms for the disease. Researchers at Michigan State University are already investigating the production of genetically engineered strains of mosquito that fail to transmit the pathogen, which may ultimately allow the wild population to be replaced by this 'innocuous' strain.[2]

Epidemiological research

A study was initiated in the Soroti District of Uganda following an outbreak of *Trypanosoma brucei rhodesiense* sleeping sickness. The disease had previously been absent in the district. However, it coincided with large-scale livestock restocking activities in the area and the research investigated the role of the cattle in the origins of the outbreak, as they can form important reservoirs for the parasite.[3] This project was supported by the UK MRC and the DFID Animal Health Programme.

Natural history of diseases

In 2000, the UK MRC funded a 3-year study in north eastern Tanzania. This programme is examining how the pattern of malarial infection is affected by changes in the intensity of malaria transmission due to the effects of altitude on mosquito survival.[4]

Social and behavioural research

Members of the Kigoyera Parish in western Uganda who had undergone HIV testing and counselling were interviewed about their sexual behaviour. This study, which was supported by Germany, was conducted to examine the effectiveness of HIV counselling and testing in reducing high-risk sexual behaviour in this rural population.[5]

Clinical research

The US company, VaxGen is currently conducting a phase III placebo-controlled, double blind trial of its HIV vaccine in Thailand. The participants in research are HIV-negative injecting drug users with a high risk of blood-borne HIV transmission. The trial is designed for a total of 2500 volunteers and is taking place in 17 methadone clinics under the direction of the Bangkok Metropolitan Administration.[6]

Feasibility studies

It was proposed that Zimbabwe adopt a visual inspection with acetic acid (vinegar) as a first line low cost screening method for cervical cancer. A feasibility study was planned in two districts of Zimbabwe to assess the feasibility of integrating the inspection into existing primary health care facilities.[7] This research was supported by the Ministry of Health of Zimbabwe and the United Nations Population Fund (UNFPA).

BOX 2.1 *Continued*

Health systems research

The International Trachoma Initiative (ITI)[8] is dedicated to eliminating blindness from trachoma. This is a preventive and treatment-based programme, involving the donation of the medicine Zithromax (Azithromycin) and supplemented by surgical techniques and public hygiene education. The programme is then followed up to determine its effectiveness. To date, studies have been conducted in Morocco and Tanzania to assess its success.[9]

1 Catteruccia F, Nolan T, Loukeris TG, Blass C, Savakis C, Kafatos FC *et al* (2000) Stable germline transformation of the malaria mosquito *Anopheles stephensi*, **Nature**, 405: 959–62.
2 Scientists are racing to create a genetically modified 'super mosquito' that will destroy malaria …, **Sunday Times**, 1 July 2001.
3 See Fevre EM, Coleman PG, Odiit M, Magona JW, Welburn SC and Woolhouse ME (2001) The origins of a new Trypanosoma brucei rhodesiense sleeping sickness outbreak in eastern Uganda, **Lancet**, 358(9282) 625–8.
4 See http://makeashorterlink.com/?C2684108.
5 See Kipp W, Kabagambe G and Konde-Lule J (2001) Low impact of a community-wide HIV testing and counseling program on sexual behavior in rural Uganda, **AIDS Education and Prevention**, 13(3) 279–89.
6 See 'VaxGen Clinical Trials' at http://www.vaxgen.com/vaccine/index.html.
7 http://www.south-south.org/Word_pdf/Sstories/Jinja/cervical%20cancer.pdf.
8 The ITI was established by Pfizer Inc. and the Edna McConnell Clark Foundation.
9 Access to medicines in the developing world through partnerships, comments by Chuck Hardwick, Senior Vice President, Pfizer Inc., WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs, 10 April 2001, Høsbjør, Norway.

health policy in their own country.[25] Others have used approaches developed over the past decade to systematise the setting of priorities in research on health. The broad aim of these initiatives has been to enable decision makers to make more informed decisions in their allocation of limited research funds. The specific objective has been to ensure that a given investment in research has the greatest impact on the health of the largest number of people in the community. However, many developing countries do not have the resources to make a comprehensive assessment of the prevalence and effects of disease within their borders.

2.23 Essential national health research (ENHR) is a strategy which has been used by several developing countries to organise and manage research related to healthcare through systematic priority setting.[26] Key criteria for the selection of research areas for priority include economic impact, cost effectiveness of future interventions, effect on equity, social justice and acceptability, and contribution to the strengthening of capacity in research. Some 18 countries have developed ENHR strategies including South Africa, Thailand, Pakistan and Tanzania. The implementation of these strategies will depend on several factors, not least research capacity, the availability of adequate infrastructure and the availability of funding.

25 WHO's recommendations about priority areas are formulated by The UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), its research programmes and by the Joint United Nations Programme on HIV/AIDS (UNAIDS). More than 50 developing countries have additionally adopted ENHR strategies to support action promoting equity in health. Countries have used a variety of mechanisms to implement the ENHR strategy but which share a common link between research and policymaking. For example, Jamaica has had an ENHR Task Force in place since 1995 which is formally recognised by the Ministry of Health and brings together representatives from the Ministry, university-based units, and the Planning Institute of Jamaica in promoting and advocating ENHR. Uganda has a national task force which consults on research priorities with senior government officials and researchers, district planning committees and health teams, along with community members. In addition, Uganda's ENHR co-ordinating team is trying to develop the capacity to set research priorities and carry out relevant research at the district level, to allow better definition of district-specific problems and the contribution of local communities in determining such. (See Neufeld V and Johnson N (2001) Forging Links for Health Research. Perspectives from the Council on Health Research for Development, International Development Research Center, Canada for further details of country-specific initiatives.)
26 The concept of ENHR was advanced by the Commission of Health Research for Development (1990) and its successor, the Task Force on Health Research for Development (1991). The Council on Health Research for Development (COHRED) has further developed the approach through practical application in several countries and provides the current mechanism of support for ENHR at the country and global level.

2.24 Overall, progress in implementing strategies for ENHR has been slow and uneven for a number of reasons, including ineffective strategies for communication and weak national funding arrangements. The sociopolitical realities of some countries or parts of countries have also been cited as problematic in establishing effective links between research and policy, whilst international organisations involved in research on health may also significantly influence what happens within a recipient country.[27] It has been suggested that these strategies for priority setting have only had an impact in countries such as Thailand where some national funding has been committed to subsequent implementation.[28] In countries where nearly all research related to healthcare is externally funded, the priorities for research have been largely set by the external sponsors.

2.25 In such circumstances, questions arise about the extent to which external sponsors are guided by national priorities when making decisions about research sponsorship. External agencies, including other national governments, research councils, private sponsors, non-governmental institutions or agencies and pharmaceutical companies, sponsor the majority of research related to healthcare in developing countries. Many funding agencies have their own approaches for the identification of areas which merit support. As many external sponsors fund at the level of individual researchers rather than institutions, it is important that there is awareness of priorities for national research at the local level.

2.26 Governmental bodies such as the UK Medical Research Council (MRC) and UK Department for International Development (DfID), US Centers for Disease Control (CDC), the European Commission (EC) (see Box 2.2), international agencies and pharmaceutical companies generally support or undertake applied health-driven research, as do the large charities (for example, the Bill and Melinda Gates Foundation and the Wellcome Trust) (see Box 2.3). Scientific excellence is the first criterion used by most sponsors of research. Additional criteria for funding include the relevance of research to the host countries' needs; the practicalities of undertaking the proposed research; and the likelihood of the research results being taken up in the host country for the improvement of health. Several sponsors have advisory panels with members from both developed and developing countries to assist them in identifying areas of priority for support in consultation with the relevant communities.[29]

2.27 Several GPPPs have also been established to address the public health problems of developing countries, some of which are concerned with research or have a research component.[30] Other GPPPs are focused on the development of products such as the International AIDS Vaccine Initiative (IAVI), the Malaria Vaccine Initiative (MVI) and MMV; others are concerned with the donation of specific products such as the Malarone (antimalarial medicine) donation programme or broader programmes as in the Case of Global Alliance for Vaccines and Immunization (GAVI) (see Box 2.4). GPPPs, such as MMV and IAVI, bring together the substantial resources of public and private sector organisations to develop vaccines and medicines for common and serious diseases such as AIDS, TB and malaria.[31] Research on these diseases will clearly be relevant to the national research priorities of the majority of developing countries.

2.28 The United Nations Development Programme/World Bank/WHO 'Special Programme for Research and Training in Tropical Diseases' (TDR) is one of the international agencies that has

27 Chunharas S 'Linking research to policy and action' in Neufeld V and Johnson N (2001) **Forging Links for Health Research. Perspectives from the Council on Health Research for Development**, IDRC, Ottawa.
28 Binka F (2001) Personal communication, Navrongo Health Research Centre.
29 For example, the UK Medical Research Council and the Wellcome Trust.
30 There is some disagreement about what constitutes a public–private partnership but a good definition is thought to comprise three key components: involvement of at least one private profit-seeking organisation with at least one not-for-profit organisation; shared efforts and benefits; commitment to the creation of a social value (improved health), especially for disadvantaged countries. See Reich M (2000) Public–private partnerships for public health, **Nature Medicine**, 6(6) 617–20.
31 Lucas A (2000) Public–private partnerships. Illustrative examples, **Workshop on Public-Private Partnerships in Public Health**, 7–8 April 2000, Endicott House, Dedham, Massachusetts.

BOX 2.2 Examples of governmental bodies funding research in developing countries

UK Medical Research Council (MRC)

The UK MRC works closely with DfID to fund research relevant to priorities in healthcare in developing countries. Research funded ranges from basic to clinical research, with particular emphases given to poverty reduction and the need to foster local capacity in research through in-work training and collaborative partnerships with developing countries. The MRC has laboratories in The Gambia which undertake research programmes spanning HIV/AIDS, TB, malaria, reproductive health, viral diseases, respiratory infections, non-communicable diseases and nutrition, each having basic, clinical and epidemiological components. Additionally, the MRC has an integrated multidisciplinary research programme for the study of HIV-1 in Uganda and a malaria programme in Tanzania. The MRC's Human Immunology Unit at Oxford University has an established programme for the preparation and trials of HIV vaccines in the UK and Kenya. Phase I trials of a resultant DNA vaccine against HIV are underway in Oxford and Nairobi, Kenya.[1]

European Commission Programme of Action to combat HIV/AIDS, malaria and tuberculosis

In February 2001, the EC approved a Communication outlining a programme for action on HIV/AIDS, malaria and tuberculosis which would build on existing EC investments in research on these major diseases.[2] In terms of research and development, this emphasised targeted action for increased public support for R&D, involving continued and increased support for basic and strategic research with improved co-ordination at European and international levels, along with the creation of a European Clinical Trials platform to increase the number, efficiency and coherence of clinical trials conducted by the public and private sectors, and involving developing countries. Emphasis was also given to developing expertise in research in terms of increasing support to a range of research activities, giving emphasis to gender balance and poverty reduction and ensuring appropriate ethical standards and review systems are in place. Support would also be provided to developing countries to allow them to host and conduct large-scale population trials. The need to develop an incentive package to increase private investment in R&D for new products to tackle major communicable diseases in developing countries was also highlighted.

1 For more detailed information about the MRC's programmes in developing countries see: http://makeashorterlink.com/?C2684108.

2 See European Commission (2001) **Communication from the Commission to the Council and the European Parliament. Programme for Action: Accelerated action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction** at http://makeashorterlink.com/?I66F21E5.

sought to promote public-private partnerships, and to assist pharmaceutical companies in the late stage of product development. Acting as a broker linking academia, governments, industry, health professionals and affected communities, TDR has been involved in the implementation of field trials and the licensing out of new products, or new uses for existing products.[32]

Pharmaceutical R&D in developing countries

2.29 Most of the collaborative research undertaken by pharmaceutical companies in developing countries involves clinical trials. Priorities for national research may be considered to have little

32 Examples are multi-drug therapy for leprosy, ivermectin for onchocerciasis, eflornithine for African trypanosomiasis, artemether for malaria, praziquantel combinations for schistosomiasis and intestinal parasites, and more recently, miltefosine for visceral leishmaniasis, and artesunate suppository, medicine combinations and lapdap for malaria, among others Morel CM (2000) Reaching maturity – 25 years of the TDR, **Parasitology Today**, 16(12) 522–8.

relevance by a company that wishes to test a new medicine. Instead, the criteria for selecting a particular country for trial include the availability of suitable participants, the availability of high quality collaborators, and appropriate infrastructure for delivery of clinical care to the participants. The national priorities for research related to healthcare identified by a host country may have little bearing on where a company decides to locate its clinical trials. However, some companies such as GlaxoSmithKline (GSK) have several R&D projects to develop medicines for the treatment of diseases prevalent in developing countries (see Box 2.5). In some instances, the diseases are also relevant to developed country markets while in others, the research sponsorship may be altruistic.

2.30 Where an external agency has its own priorities for research on healthcare, provided that these coincide with those of the recipient country, there is potential for mutual benefit. If the agendas do not coincide, then the financial influence of the external agency may become the driving force (see paragraph 2.24). The principal manner in which a research sponsor might distort the priorities for research in a developing country is through the funding of research that has no direct benefit to its individuals nor to the society as a whole. Examples include the study of the natural history of a disease, a clinical intervention, a diagnostic process or the removal of tissues for research in a developed country. The example of the research on Burkitt's lymphoma in Africa (see Box 2.6) illustrates the issues which can arise when a researcher pursues a study of legitimate interest but which does not address a priority for healthcare in the host country. However, such research can offer considerable indirect benefits to host countries in the developing world because of the potential for strengthening the national capacity in research, in the form of improved infrastructure and training.

BOX 2.3 Examples of charities funding research in developing countries

Bill and Melinda Gates Foundation

In 2000, the Foundation paid and awarded grants totalling US$1240 million for global health projects. Grants awarded included funding for the development of a vaccine for leishmaniasis, funding for a feasibility study to improve the manufacturing and delivery of vaccines in Russia, support for research aimed at the reduction of child mortality and funding to promote the discovery and development of antimalarial medicines.[1]

The Wellcome Trust

The Trust has three international programmes: International Biomedical, Tropical Medicine and Population Studies programmes.[2] The Trust spent £72.2 million on international research during 1999/2000. This included research into infectious and non-infectious human diseases and veterinary problems affecting developing countries, with research primarily conducted in South-East Asia and Kenya. Several project grants were awarded as part of the Non-communicable Disease Initiative in the areas of mental health, stroke and hypertension in Africa, Latin America and Southern Asia, and additionally, a major programme grant was given in India to explore the role of maternal nutrition and the development of insulin resistance in offspring.[3]

1 See http://www.gatesfoundation.org/.
2 Within its three international programmes, the Trust awarded a variety of fellowships and research and career awards.
3 Material taken from The Wellcome Trust Annual Review 1999/2000 at http://www.wellcome.ac.uk/en/1/awtpubreparvr00int.html.

2.31 Despite the difficulties that developing countries may face in achieving the effective implementation of national priorities for research in healthcare, there is a strong case to be made for setting research priorities together with a robust mechanism for scientific review and ethical review of any proposed research (see Chapter 8). How this is managed will depend on the resources available in each country. **We therefore endorse the view of the Commission on**

BOX 2.4 Global Alliance for Vaccines and Immunization (GAVI)

GAVI has identified three priorities for its initial vaccine development efforts: pneumococcal conjugate vaccines for pneumonia and meningitis, rotavirus oral vaccines for severe diarrhoea and meningococcal A (or A/C) conjugate vaccines for meningitis. These products were selected because of their potential impact on children's health and because availability and use could be predicted in 5–7 years.[1]

1 See http://www.vaccinealliance.org/reference/ update_ agendas.html for further details about GAVI's agenda to accelerate the development and introduction of these vaccines.

BOX 2.5 GlaxoSmithKline (GSK)

GSK has more than 20 active R&D projects for medicines to treat diseases prevalent in developing countries. It has been researching vaccines for HIV, TB and malaria, has three anti-malarial products at various stages of development and clinical projects are underway with a new combination product and a novel protease inhibitor for HIV/AIDS, along with research efforts to discover medicines with novel mechanisms. GSK has an R&D programme to develop a Hepatitis E vaccine, a disease prevalent in South-East Asia. It also has a randomised clinical trial in children of Zentel (Albendazole) to assess the impact of early de-worming on long-term childhood survival.[1] In addition, GSK has more than 30 external partners and alliances for diseases relevant to developing countries. Paediatric clinical trials of a malaria vaccine began in the Gambia in May 2001 in partnership with MVI. This is the first of a series of three planned trials. GSK is also working in partnership with academic institutions and with NIH funding to identify novel targets for antimycobacterial chemotherapy and developing new compounds suitable for pre-clinical evaluation for TB.[2]

1 GlaxoSmithKline (2001) **Facing the Challenge. Our contribution to improving healthcare in the developing world**, GlaxoSmithKline plc, Greenford.

2 European Federation of Pharmaceutical Industries and Associations (EFPIA) (2001) **Non-exhaustive list of initiatives carried out by the pharmaceutical industry to combat health problems in the developing world**, EFPIA, Brussels.

Health Research for Development (1990) and its successor, the Task Force on Health Research for Development (1991) that all countries should set priorities for research into healthcare. However, given that in many developing countries, most research on healthcare is externally funded, we consider that sponsors have a responsibility to consider their own research priorities in the light of national priorities which exist in host countries.

2.32 We do not take the view that all externally-funded research should fall within nationally defined priorities, since all research contributes to the development of local skills and expertise in research, quite apart from the inherent value in diversity of research. However, there is a careful balance to be drawn. The inherent inequalities of power and advantage between developed and developing countries require that particular care is needed to restrain any tendency on the part of the sponsor to pursue their interests to the detriment of those of the host country. **We therefore recommend that when research funded by external sponsors is proposed which falls outside the national priorities for research into healthcare set by a host country, those proposing the research be required to justify the choice of the research topic to the appropriate research ethics committees in both the host and sponsoring countries.**

Developing new interventions

2.33 As we have seen, socio-economic development is usually, although not always, associated with an increase in life expectancy and reductions in the many causes of morbidity. In general, improvements in healthcare can be brought about more rapidly than improvements in socio-economic status, although the two are closely linked. While it is clear that poverty is a major

determinant of ill-health, there is increasing evidence that poor health significantly impedes development.[33] Consequently, there has been a drive to find more effective medicines and vaccines for the treatment and prevention of some of the major diseases afflicting people in developing countries. The development of such interventions may have the dual effect of directly promoting improved health and leading to further health gains through the impact that such improvements will have on socio-economic development. However, some have argued that such a focus may distract attention from interventions directed at reducing socio-economic inequalities as the fundamental means of improving health.

BOX 2.6 Burkitt's lymphoma

Burkitt's lymphoma is a childhood tumour first described in 1958. The disease is rare in Western countries but endemic to African countries such as Kenya and Uganda. Burkitt's lymphoma accounts for over half of all childhood cancers in Africa, affecting about two in 100,000 children each year. However, it is a rare cause of death when compared to diseases such as malaria (which causes to 20% of childhood deaths in the worst affected areas).

Despite its rarity, Burkitt's lymphoma was comprehensively researched in the 1950s and 60s in Africa. A team of researchers led by Burkitt charted its occurrence from Uganda to South Africa, determined the altitude-dependency of the disease, its common occurrence in malaria-endemic areas and its association with the presence of antibodies to the Epstein-Barr virus. The value of this early research to subsequent cancer research and treatment is now well recognised.[1]

1 Magrath IT (1991) African Burkitt's Lymphoma. History, biology, clinical features and treatment, **American Journal of Paediatric Hematology/Oncology**, 13(2) 222–46.

2.34 Because budgets for health are very restricted in many developing countries, interventions that are to be widely deployed must be affordable. Ideally, they would be provided or purchased locally at low cost. Examples of such interventions include insecticide-impregnated bed-nets to protect against malaria, and vitamin A supplementation to reduce child mortality. In areas in which malaria is highly prevalent, it has been shown that the provision and use of insecticide-impregnated bed-nets, which cost less than $10 each, reduce child mortality rates by 20% or more.[34] In large areas of the world where there is vitamin A deficiency, the administration of a dose of this vitamin to children every four to six months, at a cost of a few pence a dose, has also been shown to reduce total child mortality rates by around 20% (although greater costs are incurred in setting up a mechanism to ensure that children regularly receive vitamin A).

2.35 In relatively common use are some interventions that may be costly but which may be supplied at subsidised prices, or free of charge, by donor agencies or organisations from developed countries. Increasingly, international agencies have been negotiating with pharmaceutical companies to obtain concessions to supply medicines and vaccines at 'affordable' cost in developing countries through tiered pricing schemes or, in some instances, by donations of products for such use. These issues are discussed further in Chapter 9. Examples of these concessions include many vaccines and the very substantial donations of medicines that have been made by pharmaceutical companies for the treatment of river blindness (onchocerciasis) with ivermectin, elephantiasis (lymphatic filariasis) with ivermectin and albendazole, trachoma with azithromycin and malaria with Malarone®. Donor agencies have also made contraceptives widely available at little or no cost in developing countries and large numbers of condoms have been supplied in an attempt to slow the spread of HIV infection.

33 Sachs and colleagues have argued strongly the latter point in respect of malaria and other diseases. For example, see Gallup JL and Sachs JD (2000) **The Economic Burden of Malaria. CID Working Paper No. 52**, John Luke Gallop, Jeffrey D Sachs and the President and Fellows of Harvard College at http://www2.cid.harvard.edu/cidwp/052.pdf

34 Lengeler C, Armstrong-Schellenberg J, D'Allesandro U, Binka F and Cattani J (1998) Relative versus absolute risk of dying reduction after using insecticide-treated nets for malaria control in Africa, **Tropical Medicine and International Health**, 3(4): 286–90.

2.36 We have noted above that for many infectious diseases affecting predominantly those in developing countries there are either no effective treatments or vaccines available, or there is a need to develop improved or new interventions. Recent advances in microbiology and biotechnology may lead to the development of new vaccines within the next decade. Not all vaccines will provide protection against the target diseases and rigorous evaluation will be needed before their use in public health programmes. Advances in biological knowledge will similarly expand the range of potential diagnostic tests and therapeutic interventions, and these will also require careful evaluation before widespread introduction and use.

2.37 There are, of course, substantial costs associated with bringing a new medicine or vaccine into use for public health.[35] In the case of most new medicines, the development costs will be borne by a pharmaceutical or biotechnology company. In the case of vaccines, global public-private partnerships such as IAVI promise to play a key role in the development of new products directed at the developing world. There are few public institutions, even in the developed countries, that are in a position to underwrite the heavy costs of developing compounds discovered in their own laboratories to the point of marketing approval. These costs and the time-scales of the development process will be reflected in the prices placed on new medicines by the companies producing them.[36] New medicines are priced to cover not only the costs of their own development, but also the costs of those potential treatments that fail in development. It is currently estimated that only one out of every 5,000 or so compounds discovered will reach the market place.[37] Of these, only a few will be major 'blockbuster' medicines which produce very high income for a company. In addition, the discovery of new medicines is based largely on the application of new technologies which requires very considerable investment in R&D. A significant proportion of the sales revenue of a major pharmaceutical company (15–18% of sales in the UK industry) is therefore ploughed back into R&D.

2.38 The high costs of development for new medicines means that the pharmaceutical industry has generally invested in R&D for medicines for diseases which affect large numbers of people who can afford to pay for treatment, such as heart diseases, respiratory diseases, inflammatory diseases and cancers. Through the development of successful medicines for these diseases, companies aim to recover their costs, invest in further R&D and return profits to the shareholders. Consequently, diseases which affect only small numbers of patients, or which affect large numbers of patients who have no resources in their healthcare system to buy new medicines, have tended to be ignored. The small market (in terms of purchasing power, rather than population size) cannot support the effort required to bring a medicine from the laboratory to the clinic.

2.39 These are the so-called 'neglected diseases' and include many of the major tropical diseases, as well as diseases which only affect small numbers of people in developed and developing countries. For example, Table 2.4 lists the limitations of the current medications available to

35 Pharmaceutical companies have estimated this cost to be in excess of $500 million. In contrast, a recent study by Tufts Center for the Study of Drug Development put the cost of the development of a new prescription medicine at $802 million (see Tufts Center for the Study of Drug Development press release 'Tufts Center for the Study of Drug Development Pegs Cost of a New Prescription Medicine at $802 million at http://www.tufts.edu/med/csdd/images/NewsRelease113001pm.pdf). Public Citizen claimed that the figure was actually in the order of $110 million (see Public Citizen (2001) **Rx R&D Myths: The Case Against the Drug Industry's R&D 'Scare Card'**) and that the estimate of pharmaceutical companies was unreliable as it included the cost of all failed medicines, the expense of using money for research into medicines rather than other investments and did not account for the tax reductions companies obtain for R&D. However the validity of Public Citizen's claims have been challenged and attributed to'methodological shortcomings' (see Ernst and Young (2001) **Pharmaceutical Industry R&D Costs: Key Findings about the Public Citizen Report**).

36 However, other factors will also come into play in the determination of pricing. The longer the development time for the new product, the shorter the unexpired patent life when it reaches the market. The period of exclusive sales during which development costs can be recovered is therefore shorter.

37 Spilker BA 'The Drug Development and Approval Process', PhRMA at http://www.phrma.org/searchcures/newmeds/devapprovprocess.phtml. This is based on research carried out by Tufts Center for the Study of Drug Development which looked at medicines approved for the period 1993–1995 and found that only five in five thousand compounds entering preclinical testing reached testing in humans and only one in five of those tested in humans was approved for sale.

Table 2.4

Limitations of medicines for malaria

Medicine	Year of approval or use	Limitations
Quinine	1800s	Difficulties of use and effectiveness due to long treatment regimen and safety issues (e.g. tinnitus).
Chloroquine	1947	Increasing levels of parasite resistance have developed to this treatment.
SP (Fansidar)	1969	Increasing levels of parasite resistance have developed to this treatment and there are some side effects.
Artemisinins	1970s onwards	Difficulties of use and effectiveness as a single agent related to short half-life and long treatment regimen. Primarily promoted for use in combinations with other treatments, but this generates issues of compliance. Limited manufacture to the standards of good manufacturing practice. Some outstanding safety concerns but clinical experience on the whole is positive.
Mefloquine	1985	Relatively expensive, in some areas there is parasite resistance to this treatment and there are concerns about its safety.
Halofantrine	1988	Extremely expensive, some forms of malaria are resistant to this treatment and there are serious cardiotoxicity-related concerns about its safety.
Malarone	1996	Prohibitively expensive. Efficacious but there is the potential for forms of malaria to become resistant to this medicine. There is already resistance to individual components of the combination medicine.
Co-artemether	1998	Relatively expensive. Efficacious but there is the potential for resistance to develop.

treat malaria, a disease which was estimated to cause the loss of 45 million DALYs in 1999.[38] In 1996, the market for antimalarials was estimated at US$100–200 million while the market for antibacterials was over US$16,000 million (three products had sales of over US$800 million). While only one to two antimalarials are developed each decade, three to four new antibacterials reach the market each year. Moreover, of the antimalarials that have been developed, many cannot be afforded by patients in developing countries and are largely limited to the tourist market. Recently, however, as we have seen, there have been some promising developments in the area of public–private partnerships (see paragraph 6.27).

2.40 Pharmaceutical companies, encouraged by international agencies, are also starting to look for more economical, but effective, ways of using existing medicines to control diseases such as HIV/AIDS. For example, very recently, companies have begun to adapt their pricing structure to enable developing nations to receive medicines for HIV/AIDS at a fraction of the market price in the developed world, or at no cost, and there is increasing pressure on these companies to continue down this route. The World Trade Organisation (WTO) has recently clarified the position of its members with regard to their rights to implement the compulsory licensing of patented medicines when there is a public health emergency. Under such circumstances countries may manufacture generic[39] versions of patented medicines although countries without manufacturing capacity may not import these medicines.[40] However, the costs of many generic medicines will remain beyond the healthcare budgets of the majority of developing countries. In the case of antiretrovirals for

38 WHO (2000) Annex Table 4: Burden of disease in disability-adjusted life years (DALYs) by cause, sex and mortality stratum in WHO regions, estimates for 1999: 170.

39 Generic medicines are chemically the same as brand name medicines. They have the same characteristics (e.g. intended use, dosage, route of administration, safety, and quality) but are typically much lower in price than their branded counterparts.

40 World Trade Organization (2001) **Declaration on the TRIPS Agreement and Public Health (Doha Declaration)**, WT/MIN (01)/DEC/2, World Trade Organization, Geneva.

HIV/AIDS, even if the medicines were provided at no cost, the infrastructure required for delivery and monitoring side effects would be prohibitively expensive for most of the developing world.

2.41 The costs of evaluating a potential intervention for a tropical disease are substantial and, in general, cannot be covered by a developing country alone. For evaluation studies, pharmaceutical companies often donate products for trials and other costs involved may be met by international agencies. However, once efficacy has been established, the long-term supply of a product for public health use in a developing country may be very problematic if, as is often the case, the cost is beyond the resources available in the healthcare system. The slow deployment of vaccines against hepatitis B in developing countries and the restricted use of praziquantal against schistosomiasis are such examples.

2.42 However the cost of an intervention at the time of evaluation may fall substantially in due course (see Box 1.3). There have also been examples where beneficial interventions that are relatively costly can be used to argue the case for lowering, or subsidising, the price for developing countries. For example, in The Gambia, the demonstration of a strong protective effect of a vaccine against disease due to *Haemophilus influenzae* type b (HIB), has been an important factor in the more widespread promotion and subsidy of this vaccine, despite its substantial cost.

2.43 Not all 'new' interventions are expensive, however, and perhaps some of the most important advances have been made using products that are within, or close to, the resources that might reasonably be made available locally. For example, oral rehydration solution is cheap to produce and is highly effective at reducing mortality from diarrhoeal diseases.

The future

2.44 It can be expected that in the future there will need to be a radical change in the approach of the pharmaceutical industry to its R&D programmes and its investment in research. The first phase of the human genome project is now largely completed and it is reasonable to expect that increasing numbers of genes associated with, or perhaps causing, human diseases will be identified. This will provide research scientists with potential new molecular targets for the discovery of new medicines over the longer term. This approach has the potential to provide cures where existing medicines have only been able to alleviate the symptoms of a disease. However, many diseases will have multigene substrates, and selecting the optimal molecular target will be a substantial challenge.

2.45 However, it is possible that some of the currently 'common' human diseases will in fact be found to be a collection of different diseases, sharing a common appearance, but caused by different molecular mechanisms. Several common diseases may become collections of conditions affecting much smaller populations. Each condition may require a specific treatment. However, the cost of discovery, development and registration of new medicines for each condition may change, for example as clinical trials may change in size and complexity. It follows that for some diseases or sub-sets of disease improved treatments may only be available at higher prices. Providers of healthcare in the developing and developed world will need to adapt to the new approach. They will need not only to consider the cost of the medicines but also to take account of the cost-effectiveness and outcomes of new interventions, for instance reduced hospitalisation within the overall healthcare delivery system, as well as the more general economic benefits. In developing countries these new approaches will be difficult to implement, indeed, existing infrastructure is challenged to deliver current diagnostics and medicines. For the providers of healthcare, the provision of the infrastructure required to employ 'gene-based' or pharmacogenetic[41] medicines

41 Pharmacogenetics is the study of how genetic differences influence the variability in patients' responses to medicines.

effectively, i.e. screening and diagnostics, will present yet further challenges. For those wishing to carry out clinical trials, the costs may well become prohibitive if they must provide the necessary infrastructure to undertake such research. For these reasons, the pharmacogenetic approach to the development of medicines is unlikely to be available for developing countries for the foreseeable future.